

**REMARKS**

Claims 24-39 are pending in the present application. Applicants note with appreciation that the Office has withdrawn rejection of the claims under 35 U.S.C. §112, second paragraph.

Claims 24, 30, 31 and 33 are rejected under 35 U.S.C. §102(e) as anticipated by Liberti et al. This reference is cited for teaching a coating process which results in stable, resuspendable coated particles. Applicants have amended claims 24 and 31 to incorporate the limitations of claim 25, which has not been rejected on this basis. Claims 30 and 33 depend from claims 24 and 31, respectively, and therefore also now contain these limitations. Applicants submit that this amendment obviates the Office's rejection and therefore request that the Office withdraw the rejection of claims 24, 30, 31 and 33 as anticipated by Liberti et al.

Claims 25-29, 32 and 34-39 are rejected under 35 U.S.C. §103(a) as obvious over Liberti et al. in view of Nichtl et al. The Office bases this rejection on the contention that Liberti et al. teaches a coating process for coating a wide range of materials (including detergents) onto colloidal magnetically responsive particles to obtain stable microagglomerates. Liberti et al. fail to teach, however, an additional stabilizer such as an inert protein and/or polyethylene glycol after particle coating and fail to teach gold, silver, copper, platinum or palladium particles. Nichtl et al. are cited for teaching that after the colloidal particles have been loaded with the desired biomolecule, it is necessary to stabilize the particles. This post-loading stabilization is stated to minimize aggregation of the particles and saturate remaining free surfaces.

Nichtl et al. are cited for teaching metal particles such as gold, silver, copper, platinum, palladium and mixtures thereof.

The Office concludes that it would have been obvious to add an inert protein as taught by Nichtl et al. to conjugates formed by the Liberti et al. methods.

Applicants traverse this rejection. Liberti et al. do not teach a coating material in which detergent does not adversely influence the function of the conjugates by displacing the biomolecules or by interacting with the biomolecules or the colloidal particles after loading. The Liberti et al. coatings are clearly described by the authors to "saturate the remaining free surfaces accessible to adsorption." Office Action, page 5, lines 3-4. If the coating saturates remaining free surfaces of the biomolecules, the particles or both, then it does not meet the claim limitation which requires that the detergent coating in the present invention does not adversely influence function by interacting with the biomolecules or the colloidal particles. The Liberti et al. coating interacts to the detriment of function.

The Office states that Applicants' arguments are not on point because the claims fail to require "that the stability must refer to the function of the particles." Claim 24 clearly recites that the "detergent does not adversely influence the function of the conjugates." The body of claim 24 does not refer to "stability" in general, but specifies function of the coated particles. Therefore the Office is in error on this point.

The Office points out that the claims contain "opening language," Office Action, page 6, line 17, and therefore can include "other limitations such as aggregation." Although the claims use the transitional phrase "comprising," the specific recited limitation in the claims, that the detergent does not adversely influence the function of the conjugates, is not disclosed, suggested or even hinted at in the teachings of Liberti et al. That the particles of the present invention also may be stable from agglomeration due to open claim language is not

relevant when claim limitations specifically recited in the body of the claim are completely absent from the prior art.

Further, the Office states that the role of detergent in Liberti et al. is to stabilize the particles, not to displace the biomolecules. The preferred role is not relevant when the reference teaches that, despite stability from agglomeration, the coating does interact with the particles, as the Office already has conceded. Whether stability from agglomeration is present in either the Liberti et al. particles or the inventive particles is not relevant to the claims here.

Essentially, the Office is arguing that because the Liberti et al. particles don't clump together, the coating does not interact with biomolecules or particles. The Office has conceded that the detergent coatings not only do interact with metal particles, Office Action at page 5, lines 3-4 and page 7, line 12, but that this is recognized in the art as a problem to be solved, Office Action at page 7, lines 12-13.

Finally, the Office states that "Nichtl therefore teaches away from using detergents in biomolecule-particle conjugates as the present claims require," Office Action at page 7, lines 13-15, but relies on the Nichtl et al. reference for use of stabilizer, not detergents. \*It is not permissible for the Office to pick and choose among the teachings of a reference, ignoring certain clear teachings in the reference, to cobble together a rejection. See M.P.E.P. §2141, Basic Consideration Which Apply to Obviousness Rejections ("references must be considered as a whole"). \* "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." M.P.E.P. §2141.02 (emphasis in original); W.L. Gore & Assoc., Inc. v. Garlock, Inc. 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984).

Here, the Office has admitted that Nichtl et al. teach away from the invention as recited in the claims, but nevertheless rejects the claims on the basis of this reference's other teachings alone, improperly ignoring teachings that not only calls into serious question the Office's interpretation of the primary reference, but also clearly shows that there can be no motivation whatsoever to combine the cited references.


To make out a prima facie case of obviousness, the Office must meet three criteria (1) the cited art must teach or suggest each and every limitation of the rejected claims; (2) there must be motivation to make the combination in the references or in the art generally; and (3) there must be a reasonable expectation of success. The Office has not met even one criterion in this case. (1) The art as a whole does not teach or suggest using detergents which do not adversely influence the function of conjugates because Liberti et al. shows and the Office has admitted that these prior art coatings do interact with the particles and because Nichtl et al. teach away from use of detergents in these coated particles, showing even more clearly that the Liberti et al. particles are adversely influenced as to function. (2) The teachings of Nichtl et al. would not be combined with those of Liberti et al. because Nichtl teaches away from using detergents as required by the present claims and as suggested by Liberti et al. This clear teaching cannot be ignored. (3) There can be no reasonable expectation of success when combining a stabilizer of Nichtl et al. with detergents of Liberti et al. when Nichtl et al. advise against using detergents at all with their methods.

Applicants submit that the Office has not made out and cannot make out a prima facie case of obviousness against the present claims based on Liberti et al. and Nichtl et al. Applicants therefore request that the Office withdraw this rejection.



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For the above reasons, Applicants believe that the claims are in condition for allowance and request favorable consideration at this time.

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